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Room: Room 2.60

Transmission, prevention and management of drug resistant tuberculosis

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The rise of drug-resistant tuberculosis threatens the very fabric of traditional tuberculosis control efforts, particularly in South Africa, Eastern Europe and parts of Asia. Initial complacency was guided by laboratory observations which suggested that drug-resistant strains of *Mycobacterium tuberculosis* are less transmissible than drug-susceptible "wild-type" strains.

However, the fact that young children in close contact with adult drug-resistant tuberculosis patients frequently became infected and/or diseased, usually with the same strain, provided clear evidence of transmissibility. Advanced genomic analysis has since provided novel insight into the evolution and spread of drug-resistant strains, highlighting unique epidemiological features related to programmatic management in specific geographic areas.

Young children and immune compromised individuals are at high risk to develop active tuberculosis following close contact with a drug-resistant source case. Although observational data demonstrate clear benefit from contextualized post-exposure prophylaxis, formal guidance remains limited pending more robust information from large field trials.

Wide scale roll-out of the MTB/RIF Xpert® test has facilitated early diagnosis of cases with drug-resistant tuberculosis. Multiple challenges such as high cost, technical and maintenance issues, result interpretation, false positive read-outs and misassignment of multi-drug resistant (MDR) status in cases with rifampicin mono-resistance remain, especially in resource-limited settings. In addition, MDR treatment programs are inadequate and heavily dependent on external donor funding in most settings, this restricts treatment access and threatens the sustainability of programs.

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Multi-epitope peptide vaccines for human lymphatic filariasis

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Background: Human Lymphatic Filariasis, caused by the nematode parasites *W. bancrofti* and *B. malayi* infect about 128 million people in 83 countries. Filarial Thioredoxin (TRX), a multifunctional protein with antioxidant properties, plays an important role in scavenging the hydroperoxides and protects parasites from host immune system. The enzyme transglutaminase (TGA) catalyzes post translational modifications of proteins, is required for growth and development of the larval stages and has a role in *in utero* development of microfilariae in adult female. Although TRX and TGA have been proved to be promising vaccine antigens in previous studies they share ~43-63% homology with host proteins which is a major drawback for vaccine development. Hence, an attempt was made to develop peptide vaccines using B and T epitopes from host non-homologous regions of these key metabolic enzymes. Epitope-based vaccines have been extensively shown to be promising in various diseases, capable of inducing protective immunity.

Methods & Materials: In this study, nematode specific regions of TRX and TGA were screened and putative B/T cell epitopes in these host non-homologues regions were predicted by immuno-informatic analysis. Four such peptides were chemically synthesized and encapsulated in polymeric microspheres. The epitope peptides were validated by various immunological assays using mice models and human clinical samples. The epitopes were then synthesized as di-peptide conjugates in different combinations and tested for protective efficacy against L3 larval challenge in filarial experimental model.

Results: Two TRX peptides (TRX_{P1} and TRX_{P2}) were found to carry linear B cell epitopes while TGA carried a T cell epitope (TGA_{P1}) recognized both in mice and humans. The peptides were synthesized as di-peptide conjugates in two different combinations and the conjugates were evaluated for their vaccine efficacy in *Mastomys coucha* model. The peptide conjugates (PC2 and PC3) conferred high protection (71.97% and 72.73% respectively) which was found to be significantly greater ($P < 0.018$) than the recombinant proteins.

Conclusion: The study proves the potential of multi-epitope vaccines for parasitic infections that exploits epitopes from multiple stages and/or multiple antigens.

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